

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 20 JUL 2006

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To:
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference		Date of mailing (day/month/year) 17 JUL 2006
		FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US05/10212	International filing date (day/month/year) 25 March 2005 (25.03.2005)	Priority date (day/month/year) 30 March 2004 (30.03.2004)
International Patent Classification (IPC) or both national classification and IPC IPC: C07K 1/00(2006.01) USPC: 530/350		
Applicant GRYPHON THERAPEUTICS, INC.		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 07 June 2006 (07.06.2006)	Authorized officer Bruce Hissong Telephone No. (571) 272-1600
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Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/10212

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US05/10212

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 28-31

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 28-31 are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

Please See Continuation Sheet

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US05/10212

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>7-23, 26 and 32-49</u>	YES
	Claims <u>1-6, 24, 25 and 27</u>	NO
Inventive step (IS)	Claims <u>7-23, 26 and 32-49</u>	YES
	Claims <u>1-6, 24, 25 and 27</u>	NO
Industrial applicability (IA)	Claims <u>1-49</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-6, 24-25, and 27 lack novelty under PCT Article 33(2) as being anticipated by Chakravarty *et al.* The claims of the instant application are drawn to synthetic chemokines that are truncated at the C-terminus, and methods of making said synthetic chemokines, polymeric modifications to said chemokines, and methods of treatment with said chemokines. Chakravarty *et al.* teaches a C-terminal truncated chemokine, MCP-1 (see abstract and materials and methods, p. 29641 2nd column - p. 29642 1st column). Specifically, Chakravarty *et al.* teaches truncation of the 5 amino acid residues at the C-terminus, which includes a lysine residue. This truncation is C-terminal to the last disulfide forming cysteine and to the core helix region. Additionally, because only 5 amino acids were deleted, and because the metes and bounds of the term "substantially" are not defined by claim 24, the MCP-1 C-terminally truncated polypeptide of Chakravarty *et al.* would have substantial homology to the wild-type polypeptide. Although Chakravarty *et al.* does not specifically teach a *synthetic* MCP-1, the C-terminally truncated MCP-1 taught by Chakravarty *et al.* meets the limitations of the instant claims regardless of any process used.

Claims 1-6, 24-25, and 27 lack an inventive step under PCT Article 33(3) as being obvious over Chakravarty *et al.* As set forth above, claims 1-6, 24-25, and 27 lack novelty as being anticipated by Chakravarty *et al.* Because the claims lack novelty, they also lack an inventive step under PCT Article 33(3).

Claims 7-23, 26, and 32-49 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest methods of making a synthetic C-terminally truncated chemokine, polymeric modifications to said chemokine, or methods of treatment using said chemokine.

Claims 1-49 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry.